

WHAT IS CLAIMED IS:

1. A composition comprising a biologically active protein and a carrier which comprises polymeric backbone having attached positively charged branching groups and which is present in an effective amount for transdermal delivery, wherein the association between the carrier and the biologically active protein is non-covalent.
2. A composition according to claim 1 in which the therapeutic protein excludes insulin, botulinum toxins, VEGF, and antibody fragments.
3. A composition according to claim 2 in which the therapeutic protein does not therapeutically alter blood glucose levels.
4. A composition according to claim 2 in which the therapeutic protein excludes botulinum toxins.
5. A composition according to claim 2 in which the therapeutic protein excludes VEGF.
6. A composition according to claim 2 in which the therapeutic protein excludes antibody fragments.
7. A composition according to claim 1 wherein the composition provides greater transdermal delivery of the biologically active protein relative to the agent in the absence of the carrier.
8. A composition according to claim 7 in which the biologically active protein has therapeutic activity.
9. A composition according to claim 8 in which the therapeutic protein has a molecular weight of less than 20,000 kD.
10. A composition according to claim 1 in which the backbone comprises a positively charged polypeptide.
11. A composition according to claim 10 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 10,000 to about 1,500,000.
12. A composition according to claim 10 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 25,000 to about 1,200,000.

13. A composition according to claim 10 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 100,000 to about 1,000,000.
14. A composition according to claim 10 in which the backbone comprises a positively charged polylysine.
15. A composition according to claim 14 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 10,000 to about 1,500,000.
16. A composition according to claim 14 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 25,000 to about 1,200,000.
17. A composition according to claim 14 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 100,000 to about 1,000,000.
18. A composition according to claim 1 in which the backbone comprises a positively charged nonpeptidyl polymer.
19. A composition according to claim 18 in which the nonpeptidyl polymer backbone comprises a positively charged polyalkyleneimine.
20. A composition according to claim 19 in which the polyalkyleneimine is a polyethyleneimine.
21. A composition according to claim 20 in which the polyethyleneimine has a molecular weight of from about 10,000 to about 2,500,000.
22. A composition according to claim 20 in which the polyethyleneimine has a molecular weight of from about 100,000 to about 1,800,000.
23. A composition according to claim 20 in which the polyethyleneimine has a molecular weight of from about 500,000 to about 1,400,000.
24. A composition according to claim 1 in which the carrier comprises a polymeric backbone having attached positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$, HIV-TAT and fragments thereof, and Antennapedia PTD and fragments thereof, in which the subscript $n1$ is an integer of from 0 to about 20, and the subscript $n2$ is independently an odd integer of from about 5 to about 25.
25. A composition according to claim 24 in which the positively charged branching groups are selected from groups having the formula $-(\text{gly})_{n1}-(\text{arg})_{n2}$.

26. A composition according to claim 25 in which the subscript n1 is an integer of from about 1 to about 8.

27. A composition according to claim 25 in which the subscript n1 is an integer of from about 2 to about 5.

28. A composition according to claim 25 in which the subscript n2 is an odd number of from about 7 to about 17.

29. A composition according to claim 25 in which the subscript n2 is an odd number of from about 7 to about 13.

30. A composition according to claim 24 in which the branching groups are selected from HIV-TAT and fragments thereof.

31. A composition according to claim 30 in which the attached positively-charged branching groups are HIV-TAT fragments that have the formula $(\text{gly})_p\text{-RGRDDRRQRRR-(gly)}_q$, $(\text{gly})_p\text{-YGRKKRRQRRR-(gly)}_q$, or $(\text{gly})_p\text{-RKKRRQRRR-(gly)}_q$ wherein the subscripts p and q are each independently an integer of from 0 to 20.

32. A composition according to claim 24 in which the branching groups are Antennapedia PTD groups or fragments thereof.

33. A composition comprising a non-protein non-nucleotide biologically active agent and a carrier which comprises a polymeric backbone having attached positively charged branching groups and which is present in an effective amount for transdermal delivery, wherein the association between the carrier and the biologically active agent is non-covalent.

34. A composition according to claim 33 wherein the composition provides greater transdermal delivery of the biologically active agent relative to the agent in the absence of the carrier.

35. A composition according to claim 34 in which the biologically active agent has a therapeutic activity.

36. A composition according to claim 33 in which the backbone comprises a positively charged polypeptide.

37. A composition according to claim 36 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 10,000 to about 1,500,000.

38. A composition according to claim 36 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 25,000 to about 1,200,000.

39. A composition according to claim 36 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 100,000 to about 1,000,000.

40. A composition according to claim 36 in which the backbone comprises a positively charged polylysine.

41. A composition according to claim 40 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 10,000 to about 1,500,000.

42. A composition according to claim 40 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 25,000 to about 1,200,000.

43. A composition according to claim 40 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 100,000 to about 1,000,000.

44. A composition according to claim 33 in which the backbone comprises a positively charged nonpeptidyl polymer.

45. A composition according to claim 44 in which the nonpeptidyl polymer backbone comprises a positively charged polyalkyleneimine.

46. A composition according to claim 45 in which the polyalkyleneimine is a polyethyleneimine.

47. A composition according to claim 46 in which the polyethyleneimine has a molecular weight of from about 10,000 to about 2,500,000.

48. A composition according to claim 46 in which the polyethyleneimine has a molecular weight of from about 100,000 to about 1,800,000.

49. A composition according to claim 46 in which the polyethyleneimine has a molecular weight of from about 500,000 to about 1,400,000.

50. A composition according to claim 33 in which the carrier comprises a polymeric backbone having attached positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$, HIV-TAT and fragments thereof, and Antennapedia PTD

and fragments thereof, in which the subscript n_1 is an integer of from 0 to about 20, and the subscript n_2 is independently an odd integer of from about 5 to about 25.

51. A composition according to claim 50 in which the positively charged branching groups are selected from groups having the formula $-(\text{gly})_{n_1}-(\text{arg})_{n_2}$.

52. A composition according to claim 51 in which the subscript n_1 is an integer of from about 1 to about 8.

53. A composition according to claim 51 in which the subscript n_1 is an integer of from about 2 to about 5.

54. A composition according to claim 51 in which the subscript n_2 is an odd number of from about 7 to about 17.

55. A composition according to claim 51 in which the subscript n_2 is an odd number of from about 7 to about 13.

56. A composition according to claim 50 in which the branching groups are selected from HIV-TAT and fragments thereof.

57. A composition according to claim 56 in which the attached positively-charged branching groups are HIV-TAT fragments that have the formula $(\text{gly})_p\text{-RGRDDRRQRRR-(gly)}_q$, $(\text{gly})_p\text{-YGRKKRRQRRR-(gly)}_q$, or $(\text{gly})_p\text{-RKKRRQRRR-(gly)}_q$ wherein the subscripts p and q are each independently an integer of from 0 to 20.

58. A composition according to claim 50 in which the branching groups are Antennapedia PTD groups or fragments thereof.

59. A composition according to claim 33 containing from about 1×10^{-20} to about 25 weight % of the biologically active agent and from about 1×10^{-19} to about 30 weight % of the carrier.

60. A controlled release composition according to claim 33.

61. A kit for administration of a composition according to claim 1 to a subject comprising a device for delivering the biologically active agent and a carrier which comprises a polymeric backbone having attached positively charged branching groups and which is present in an effective amount for transdermal delivery.

62. A kit according to claim 60 wherein the biologically active agent excludes insulin, botulinum toxins, VEGF, and antibody fragments.

63. A kit according to claim 62 in which the composition is contained in a device for administering the biologically active protein to a subject via the skin or epithelium.

64. A kit according to claim 63 in which the device is a skin patch.

65. A kit for administration of a biologically active protein to a subject comprising a device for delivering the biologically active protein to the skin or epithelium and a composition comprising a polymeric carrier having attached positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$, HIV-TAT and fragments thereof, and Antennapedia PTD and fragments thereof, in which the subscript $n1$ is an integer of from 0 to about 20, and the subscript $n2$ is independently an odd integer of from about 5 to about 25, wherein the association between the carrier and the biologically active protein is non-covalent.

66. A kit according to claim 65 in which the device is a skin patch.

67. A method of administering a biologically active protein to a subject comprising topically applying to the skin or epithelium of the subject the protein in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged branching groups, wherein the association between the carrier and the biologically active protein is non-covalent.

68. A method according to claim 66 wherein the composition provides greater transdermal delivery of the biologically active protein relative to the agent in the absence of the carrier.

69. A method according to claim 68 in which the biologically active protein has therapeutic activity.

70. A method according to claim 69 in which the therapeutic protein excludes insulin, botulinum toxins, VEGF, and antibody fragments.

71. A method according to claim 69 in which the therapeutic protein does not therapeutically alter blood glucose levels.

72. A method according to claim 69 in which the therapeutic protein excludes a botulinum toxin.

73. A method according to claim 69 in which the therapeutic protein excludes antibody fragments.

74. A method according to claim 69 in which the therapeutic protein excludes VEGF.

75. A method of administering a non-protein non-nucleotide biologically active agent to a subject comprising topically applying to the skin or epithelium of the subject the biologically active agent in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged branching groups, wherein the association between the carrier and the biologically active agent is non-covalent.

76. A method according to claim 75 wherein the composition provides greater transdermal delivery of the biologically active agent relative to the agent in the absence of the carrier.

77. A method according to claim 76 in which the biologically active agent has a therapeutic activity.

78. A method according to claim 75 in which the biologically active protein and carrier are administered to the subject in a composition containing both components.

79. A method according to claim 75 in which the biologically active protein and carrier are administered separately to the subject.

80. A method according to claim 77 in which the biologically active protein and carrier are administered to the subject in a composition containing both components.

81. A method according to claim 77 in which the biologically active agent and carrier are administered separately to the subject.

82. A method according to claim 75 in which the composition is a controlled release composition.

83. A method according to claim 77 in which the composition is a controlled release composition.

84. A method according to claim 75 in which the non-protein non-nucleotide biologically active agent is antifungal agent.

85. A composition according to claim 33 in which a biologically active agent is an antifungal agent.

86. A composition according to claim 85 containing from about 1×10^{-10} to about 49.9 weight % of the biologically active agent and from about 1×10^{-9} to about 50 weight % of the carrier.

87. A controlled release composition according to claim 85.

88. A composition according to claim 85 in which the antifungal agent is selected from amphotericin B, fluconazole, flucytosine, itraconazole, ketoconazole, clotrimazole, econazole, griseofulvin, miconazole, nystatin, ciclopirox and the like.

89. A kit for administration of a non-protein non-nucleotide biologically active agent to a subject comprising a device for delivering the agent to the skin or epithelium of the subject and a composition according to claim 33.

90. A kit according to claim 89 further comprising a custom applicator.

91. A kit according to claim 89 in which the agent is an antifungal agent and the composition is contained in a device for administering an antifungal agent to a subject via the nail plate or adjacent anatomic structures.

92. A kit according to claim 89 in which the device is a prosthetic nail plate or lacquer.

93. A method according to claim 75 in which the biologically active agent is an agent for treating or preventing symptoms of psoriasis.

94. A method according to claim 84 in which an antifungal agent and carrier are administered to the subject in a composition containing both components.

95. A method according to claim 84 in which the antifungal agent and carrier are administered separately to the subject.

96. A method according to claim 84 in which the composition is a controlled release composition.

97. A method according to claim 84 in which the antifungal agent is selective from amphotericin B, fluconazole, flucytosine, itraconazole, ketoconazole, clotrimazole, econazole, griseofulvin, miconazole, nystatin, ciclopirox and the like.

98. A method according to claim 84 in which the antifungal agent is administered to treat the symptoms and signs of a fungal infection.

99. A method according to claim 84 in which the antifungal agent is administered to alter symptoms or signs of fungal infection of the nail plate or nail bed.

100. A composition comprising an antigen suitable for immunization and a carrier which comprises a polymeric backbone having attached positively charged branching groups and which is present in an effective amount for transdermal delivery, wherein the association between the carrier and the antigen is non-covalent.

101. A composition according to claim 100 in which the backbone comprises a positively charged polypeptide.

102. A composition according to claim 101 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 10,000 to about 1,500,000.

103. A composition according to claim 101 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 25,000 to about 1,200,000.

104. A composition according to claim 101 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 100,000 to about 1,000,000.

105. A composition according to claim 101 in which the backbone comprises a positively charged polylysine.

106. A composition according to claim 105 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 10,000 to about 1,500,000.

107. A composition according to claim 105 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 25,000 to about 1,200,000.

108. A composition according to claim 105 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 100,000 to about 1,000,000.

109. A composition according to claim 100 in which the backbone comprises a positively charged nonpeptidyl polymer:—

110. A composition according to claim 109 in which the nonpeptidyl polymer backbone comprises a positively charged polyalkyleneimine.

111. A composition according to claim 110 in which the polyalkyleneimine is a polyethyleneimine.

112. A composition according to claim 111 in which the polyethyleneimine has a molecular weight of from about 10,000 to about 2,500,000.

113. A composition according to claim 111 in which the polyethyleneimine has a molecular weight of from about 100,000 to about 1,800,000.

114. A composition according to claim 111 in which the polyethyleneimine has a molecular weight of from about 500,000 to about 1,400,000.

115. A composition according to claim 100 in which the carrier comprises a polymeric backbone having attached positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$, HIV-TAT and fragments thereof, and Antennapedia PTD, in which the subscript $n1$ is an integer of from 0 to about 20, and the subscript $n2$ is independently an odd integer of from about 5 to about 25.

116. A composition according to claim 115 in which the positively charged branching groups are selected from groups having the formula $-(\text{gly})_{n1}-(\text{arg})_{n2}$.

117. A composition according to claim 116 in which the subscript $n1$ is an integer of from about 1 to about 8.

118. A composition according to claim 116 in which the subscript $n1$ is an integer of from about 2 to about 5.

119. A composition according to claim 116 in which the subscript $n2$ is an odd number of from about 7 to about 17.

120. A composition according to claim 116 in which the subscript $n2$ is an odd number of from about 7 to about 13.

121. A composition according to claim 115 in which the branching groups are selected from HIV-TAT and fragments thereof.

122. A composition according to claim 121 in which the attached positively-charged branching groups are HIV-TAT fragments that have the formula $(\text{gly})_p\text{-RGRDDRRQRRR-(gly)}_q$, $(\text{gly})_p\text{-YGRKKRRQRRR-(gly)}_q$, or $(\text{gly})_p\text{-RKKRRQRRR-(gly)}_q$ wherein the subscripts p and q are each independently an integer of from 0 to 20.

123. A composition according to claim 115 in which the branching groups are Antennapedia PTD groups.

124. A composition according to claim 115 in which the positively charged polymer comprises a polypeptide.

125. A composition according to claim 124 in which the polypeptide is selected from polylysines, polyarginines, polyornithines, and polyhomoarginines.

126. A composition according to claim 125 in which the polypeptide is a polylysine.

127. A composition according to claim 115 in which the polymer comprises a positively charged nonpeptidyl polymer.

128. A composition according to claim 127 in which the nonpeptidyl polymer comprises a positively charged polyalkyleneimine.

129. A composition according to claim 128 in which the polyalkyleneimine is a polyethyleneimine.

130. A composition according to claim 100 containing from about 1×10^{-10} to about 49.9 weight % of the antigen and from about 1×10^{-9} to about 50 weight % of the carrier.

131. A controlled release composition according to claim 100.

132. A composition according to claim 100 in which the antigen excludes insulin, botulinum toxins, VEGF, and antibody fragments.

133. A composition according to claim 100 in which the antigen is suitable for childhood immunizations.

134. A kit for administration of an antigen suitable for immunization to a subject comprising a device for delivering the antigen suitable for immunization to the skin or epithelium and a composition comprising a carrier consisting of a polymeric backbone having attached positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$, HIV-TAT and fragments thereof, and Antennapedia PTD, in which the subscript $n1$ is an integer of from 0 to about 20, and the subscript $n2$ is independently an odd integer of from about 5 to about 25, wherein the association between the carrier and the antigen is non-covalent.

135. A kit for administration of an antigen suitable for immunization to a subject comprising a device for delivering the antigen to the skin or epithelium and a composition according to claim 100.

136. A kit according to claim 134 further comprising a custom applicator.

137. A kit according to claim 134 in which the composition is contained in a device for administering an antigen suitable for immunization to a subject via the skin or epithelium.

138. A kit according to claim 134 in which the device is applied topically.

139. A kit according to claim 134 in which the device is a skin patch.

140. A method of administering an antigen suitable for immunization to a subject comprising topically applying to the skin or epithelium of the subject the antigen

suitable for immunization in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged branching groups, wherein the association between the carrier and the antigen is non-covalent.

141. A method according to claim 140 in which the antigen suitable for immunization and carrier are administered to the subject in a composition containing both components.

142. A method according to claim 140 in which the antigen suitable for immunization and carrier are administered separately to the subject.

143. A method according to claim 140 in which the backbone comprises a positively charged polypeptide.

144. A method according to claim 143 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 10,000 to about 1,500,000.

145. A method according to claim 143 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 25,000 to about 1,200,000.

146. A method according to claim 143 in which the backbone comprises a positively charged polypeptide having a molecular weight of from about 100,000 to about 1,000,000.

147. A method according to claim 143 in which the backbone comprises a positively charged polylysine.

148. A method according to claim 147 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 10,000 to about 1,500,000.

149. A method according to claim 147 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 25,000 to about 1,200,000.

150. A method according to claim 147 in which the backbone comprises a positively charged polylysine having a molecular weight of from about 100,000 to about 1,000,000.

151. A method according to claim 140 in which the backbone comprises a positively charged nonpeptidyl polymer.

152. A method according to claim 151 in which the nonpeptidyl polymer backbone comprises a positively charged polyalkyleneimine.

153. A method according to claim 152 in which the polyalkyleneimine is a polyethyleneimine.

154. A method according to claim 153 in which the polyethyleneimine has a molecular weight of from about 10,000 to about 2,500,000.

155. A method according to claim 153 in which the polyethyleneimine has a molecular weight of from about 100,000 to about 1,800,000.

156. A method according to claim 153 in which the polyethyleneimine has a molecular weight of from about 500,000 to about 1,400,000.

157. A method according to claim 140 in which the carrier comprises a polymeric backbone having attached positively charged branching groups selected from $-(\text{gly})_{n1}-(\text{arg})_{n2}$, HIV-TAT and fragments thereof, and Antennapedia PTD, in which the subscript $n1$ is an integer of from 0 to about 20, and the subscript $n2$ is independently an odd integer of from about 5 to about 25.

158. A method according to claim 157 in which the positively charged branching groups are selected from groups having the formula $-(\text{gly})_{n1}-(\text{arg})_{n2}$.

159. A method according to claim 158 in which the subscript $n1$ is an integer of from about 1 to about 8.

160. A method according to claim 158 in which the subscript $n1$ is an integer of from about 2 to about 5.

161. A method according to claim 158 in which the-subscript $n2$ is an odd number of from about 7 to about 17.

162. A method according to claim 158 in which the subscript $n2$ is an odd number of from about 7 to about 13.

163. A method according to claim 157 in which the branching groups are selected from HIV-TAT and fragments thereof.

164. A method according to claim 163 in which the attached positively-charged branching groups are HIV-TAT fragments that have the formula $(\text{gly})_p\text{-RGRDDRRQRRR-(gly)}_q$, $(\text{gly})_p\text{-YGRKKRRQRRR-(gly)}_q$, or $(\text{gly})_p\text{-RKKRRQRRR-(gly)}_q$ wherein the subscripts p and q are each independently an integer of from 0 to 20.

165. A method according to claim 157 in which the branching groups are Antennapedia PTD groups.

166. A method according to claim 157 in which the positively charged polymer comprises a polypeptide.

167. A method according to claim 166 in which the polypeptide is selected from polylysines, polyarginines, polyornithines, and polyhomoarginines.

168. A method according to claim 167 in which the polypeptide is a polylysine.

169. A method according to claim 157 in which the polymer comprises a positively charged nonpeptidyl polymer.

170. A method according to claim 169 in which the nonpeptidyl polymer comprises a positively charged polyalkyleneimine.

171. A method according to claim 170 in which the polyalkyleneimine is a polyethyleneimine.

172. A method according to claim 140 in which the composition is a controlled release composition.

173. A method according to claim 140 in which the antigen suitable for immunization excludes insulin, botulinum toxins, VEGF, and antibody fragments.

174. A method according to claim 140 in which the antigen is suitable for childhood immunizations.

175. A method according to claim 140 in which the antigen suitable for immunization is administered to provide resistance to an environmental antigen.

176. A method according to claim 140 in which the antigen suitable for immunization is administered to provide resistance to a potential pathogen

177. A method according to claim 140 in which the antigen suitable for immunization is administered to provide resistance to a potential biohazard.

178. A composition comprising an imaging moiety and a targeting agent and a carrier which comprises a polymeric backbone having attached positively charged branching groups and which is present in an effective amount for transdermal delivery, wherein the association between the carrier and the imaging moiety or targeting agent is non-covalent.

179. A composition according to claim 178 in which the imaging agent is an optical imaging agent.

180. A composition according to claim 179 in which the imaging agent is selected from Cy3, Cy3.5, Cy5, Cy5.5, Cy7, Cy7.5, Oregon green 488, Oregon green 500, Oregon, green 514, Green fluorescent protein, 6-FAM, Texas Red, Hex, TET, and HAMRA.

181. A composition according to claim 178 in which the imaging agent is suitable for magnetic resonance imaging.

182. A composition according to claim 178 in which the targeting agent recognizes melanoma.

183. A kit for administration of a composition according to claim 178 to a subject comprising a device for delivering the imaging and targeting moieties and a carrier which comprises a polymeric backbone having attached positively charged branching groups and which is present in an effective amount for transdermal delivery.

184. A method of administering an imaging moiety and a targeting agent to a subject comprising topically applying to the skin or epithelium of the subject the imaging moiety and targeting agent in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged branching groups, wherein the association between the carrier and the biologically active protein is non-covalent.

185. A method according to claim 184 in which the imaging agent is an optical imaging agent.

186. A method according to claim 185 in which the imaging agent is selected from Cy3, Cy3.5, Cy5, Cy5.5, Cy7, Cy7.5, Oregon green 488, Oregon green 500, Oregon, green 514, Green fluorescent protein, 6-FAM, Texas Red, Hex, TET, and HAMRA.

187. A method according to claim 184 in which the imaging agent is suitable for magnetic resonance imaging.

188. A method according to claim 184 in which the targeting agent recognizes melanoma.

189. A method according to claim 184 in which the composition is applied for screening of patients at risk for melanoma.

190. A method according to claim 184 in which the composition is applied to aid surgical excision of melanoma.

191. A method according to claim 184 in which the composition is applied in conjunction with photographic techniques or image analysis techniques.